

1 **REMARKS**

2 This amendment and response responds to an office action dated 1/29/04. Reconsideration of the
3 application in view of the above amendments and the following remarks is respectfully
4 requested.

5 Examiner has stated that the application contains claims directed to patentably distinct species of
6 the claimed invention, and that no claim is generic to primary species I (use of IR vibrational
7 spectroscopy) and species II (use of Raman vibrational spectroscopy). Applicant respectfully
8 submits that claim 35 claims "vibrational spectroscopy", which is generic to both IR and Raman
9 spectroscopy. The definition of "vibrational spectroscopy" will be discussed below. Applicant
10 has amended claim 47 to make clear that the cells are separated, conforming to claim 35. Since
11 claim 35 can be considered the same as amended claim 47, with the added limitation of
12 "statistically analyzing the characteristics of the cells" claim 47 is broader than claim 35.
13 Applicant assumes that the usual rules governing a restriction requirement are to be followed.
14 Applicant therefore elects claims 47-67 for examination, with traverse.

15 Claim 35 has been amended to correct typographical errors noted by Examiner. The claim has
16 not been narrowed by this amendment. Claim 47 has been amended as noted above.

17 Fig. 5 has been replaced by Fig. 5A and Fig. 5B, as required by Examiner. Original Sheet 5/7
18 and amended sheet 5/7 are attached to this fax transmission. Applicant states that red-lined
19 drawings are unnecessary to understand the separation of previous Fig. 5 into 2 parts.

20 The specification has been amended to reflect the changed fig. 5, which has been replaced by
21 figs. 5a and 5b.

22 Claims 35-67 are pending in this application. Claims 35 and 47 have been currently amended.

1 The office action states that Claims 35-38 are rejected under Section 35 U.S.C. 103(a)
2 as being unpatentable over Wang et al in view of Kosaka and /or Ito et al. Wang deals entirely
3 with stained cells. Such stains have been used for over 100 years. A stain is a molecule which
4 is attached by the investigator to a particular cell, tissue, or other biological material. In general,
5 the stain is "colored" when viewed with an ordinary optical microscope in transmission or
6 reflection. Some stains fluoresce. Stains are usually detected by electronic transitions in the
7 stain molecule. In contrast, the present specification deals with intrinsic vibrational transitions
8 of the cells themselves, without staining.

9 Wang does not show or suggest measuring the "spectrum of each cell", but rather
10 measuring a spectrum of an entity attached to the cell.

11 Wang states in col 5 lines 43-44 that his infrared source has a wavelength from 780 to
12 1500 nm (12,820- 6,666 cm^{-1}), which is in the range of many electronic transitions. In contrast,
13 vibrational transitions of 800-1700 cm^{-1} (as shown in Fig. 5A and B) are in a completely
14 different spectral region. The highest energy difference between the lowest vibrational state and
15 the first excited vibrational state of a molecule known to Applicant is in diatomic molecular
16 hydrogen, which is 4144 cm^{-1} . (The 4144 cm^{-1} vibrational mode of hydrogen can be seen in
17 Raman spectroscopy, but not in infra-red absorption spectroscopy, as such IR transitions are
18 forbidden by selection rules).

19 Examiner has presented a reference (Willard) to the gas phase spectrum of a diatomic
20 molecule to show that fluorescence is a "vibrational spectroscopy". It is indeed true that such
21 electronic spectra can be used to find the vibrational states in both ground and excited electronic
22 states of such molecules. However, Applicant states that one of skill in the art of vibrational
23 spectroscopy of biological entities would consider "vibrational spectroscopy" to be limited to the
24 transitions between vibrational states of the ground electronic state of the molecules, and to be
25 limited to Infra red and Raman spectroscopy.

26 The following websites are offered as additional support for the statement that vibrational
27 spectroscopy of biological molecules is recognized by one of skill in the art as either infra-red
28 absorption spectroscopy or Raman spectroscopy

- 1 <http://www.ijvs.com/archive.html> gives the list of titles of articles in the Internet Journal of
2 Vibrational spectroscopy. Electronic spectra are not mentioned.
- 3 http://www.youencyclopedia.net/Vibrational_spectroscopy
4 " Encyclopedia Entry for Vibrational spectroscopy
- 5 "The vibrational states of a molecule can be probed in a variety of ways. The most direct way is
6 infra-red spectroscopy because vibrational transitions typically require an amount of energy that
7 corresponds to the infrared region of the spectrum. However, Raman spectroscopy, Vibrational
8 Circular Dichroism and Electron energy loss spectroscopy also provide vibrational information. "
- 9 <http://www.photonics.com/dictionary/lookup/XQ/ASP/url.lookup/entrynum.5580/letter.v/pu/QX>
10 /lookup.htm
11 "vibrational transition
- 12 Definition:
- 13 A type of change in the energy levels of atoms within a molecule that result in lasing action.
14 Vibrational transitions are in actuality transitions between rotational levels of two vibrational
15 levels of the same electronic state."
- 16 <http://www.grc.uri.edu/programs/2002/vibrat.htm>
17 has the table of contents of a recent conference on vibrational spectroscopy. Electronic spectra
18 are not mentioned.
- 19 See also United States Patent 6,610,351
20 Shchegolikhin, et al. August 26, 2003
21 Raman-active taggants and their recognition

1 “Conventional Middle-Infrared (MIR) absorption spectroscopy, in principle, has much higher
2 analytical value compared to UV-VIS-absorption spectroscopy. Very roughly, MIR region is
3 commonly defined as electromagnetic radiation with frequencies between 5,000 and 500 cm⁻¹
4 (2.0-20.0 μ m). When a normal molecular motion such as a vibration, rotation or lattice mode
5 (as well as combination, difference, or overtone of these normal vibrations) results in a change in
6 the molecule's dipole moment, a molecule can absorb infrared radiation in this region of the
7 electromagnetic spectrum. In other words, very selective resonant absorptions of monochromatic
8 constituents of the infrared light from a broadband source by those molecular fragments of a
9 compound which oscillate with the frequencies corresponding to the frequencies of the incident
10 light are responsible for arising the infrared absorption bands. The corresponding frequencies and
11 intensities of these infrared bands, the infrared spectrum, are then used to characterize the
12 material. “

13 and

14 “Of importance, however, is the fact that MIR absorption spectroscopy, in principle, provides
15 information which is similar to that obtainable by normal Raman scattering spectroscopy. Both
16 infrared light absorption and Raman light scattering phenomena result in obtaining vibrational
17 spectra of a compound. Both these spectra are mutually superimposable, but do not constitute
18 replicas of each other. Rather, they are luckily complement each other giving a complete
19 vibrational spectrum of a compound. While any one (MIR or Raman) vibrational spectrum of the
20 two is a fingerprint of a compound and may be used for identification of the latter, the sum of the
21 two spectra gives a much more detailed fingerprint of a compound and permits considerably
22 more confident identification to be made. Moreover, as a rule of thumb, those normal vibrations
23 which are Raman-active are considerably less active in the infrared absorption spectroscopy. And
24 vice versa. It means that to facilitate identification of an unknown (or authentication of a
25 searched, but known beforehand) compound, a judicious choice of a method is desirable. “

26 In summary, neither Wang nor any art cited by examiner shows or suggests
27 “characterizing the vibrational spectrum of the light emitted from [the cells] each cell located by
28 the location means, wherein the vibrational spectrum is analyzed for indications that the cell is

1 in a cell division stage. ”

2 Therefore, claim 47 is allowable on 35 U.S.C. 103 grounds. Claim 35 is likewise
3 allowable. Dependent claims 36-46 and 48-67 are allowable by being dependent on allowable
4 independent claims. Dependent claims 36-46 and 48-67 are allowable in addition in that they
5 are inventive over their respective parent claims.

6 A Request for Continued Examination (RCE) under 37 CFR 1.114 is respectfully
7 requested. An additional fee of \$385 is required. The required fees and any insufficiency or
8 overage (except issue fees) may be debited or credited to deposit account 08/2240. A signed
9 deposit account authorization is on file for this case.

10 On the basis of the above amendments and remarks, reconsideration of this application
11 and its early allowance is respectfully requested.

12 CERTIFICATE OF FACSIMILE TRANSMISSION UNDER 37 CFR 1.8(a) and (b), 37CFR 1.86(f)-
13 I hereby certify that the following attached correspondence comprising Response and Amendment is being sent by facsimile transmission to

14 FAX NUMBER 703-308-0661 on April 29, 2004.
15 ~~703-308-0661~~ Amendment and Response (12 pp)
16 ~ 872 Amended Drawings (1 sheet)
17 - 9306 Copy of previous drawing (1 sheet)
18 RCE
19

20 Respectfully,

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